ABSTRACT OF THE DISCLOSURE

It is disclosed here that synaptotagmin I (syt I) and synaptotagmin II (syt II) are the cellular receptors for botulinum neurotoxin B (BoNT/B) that mediate the cellular entry and toxicity of BoNT/B. The BoNT/B binding domains of syt I and II are also disclosed. While syt I needs gangliosides for BoNT/B binding, syt II can bind to BoNT/B in the absence of gangliosides. Various nucleic acids and polypeptides that relate to the BoNT/B binding domain of syt I or II are disclosed. Further disclosed are methods of reducing BoNT/B toxicity, methods of identifying agents that can block the binding between BoNT/B and syt I or II, methods of identifying agents that can bind to the BoNT/B binding domain of syt I or II, and methods of detecting BoNT/B or *Clostridium botulinum*.